

Atrial Fibrillation After Cardiac Surgery

A Major Morbid Event?

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Objective

The purpose of the study was to investigate the incidence, predictors, morbidity, and mortality associated with postoperative atrial fibrillation (AF) and its impact on intensive care unit (ICU) and postoperative hospital stay in patients undergoing cardiac surgery in the Department of Veterans Affairs (VA).

Summary Background Data

Postoperative AF after open cardiac surgery is rather common. The etiology of this arrhythmia and factors responsible for its genesis are unclear, and its impact on postoperative surgical outcomes remains controversial. The purpose of this special substudy was to elucidate the incidence of postoperative AF and the factors associated with its development, as well as the impact of AF on surgical outcome.

Methods

The study population consisted of 3855 patients who underwent open cardiac surgery between September 1993 and December 1996 at 14 VA Medical Centers. Three hundred twenty-nine additional patients were excluded because of lack of complete data or presence of AF before surgery, and 3794 (98.4%) were male with a mean age of 63.7 ± 9.6 years. Operations included coronary artery bypass grafting (CABG) (3126, 81%), CABG + AVR (aortic valve replacement) (228, 5.9%), CABG + MVR (mitral valve replacement) (35, 0.9%), AVR (231, 6%), MVR (41, 1.06%), CABG + others (95, 2.46%), and others (99, 2.5%). The incidence of postoperative AF was 29.6%. Multivariate logistic regression analysis of factors found significant on univariate analysis showed the following predictors of postoperative AF: preoperative patient risk predictors: advancing age (odds ratio [OR] 1.61, 95% confidence interval [CI] 1.48–1.75, $p < 0.001$), chronic obstructive pulmonary disease (OR 1.37, 95% CI 1.12–1.66, $p < 0.001$), use of digoxin within 2 weeks before surgery (OR 1.37, 95% CI 1.10–1.70, $p < 0.003$), low resting pulse rate < 80 (OR 1.26, 95% CI 1.06–1.51, $p < 0.009$), high resting systolic blood pressure > 120 (OR 1.19, 95% CI 1.02–1.40, $p < 0.026$), intraoperative process of care predictors: cardiac venting via

right superior pulmonary vein (OR 1.42, 95% CI 1.21–1.67, $p < 0.0001$), mitral valve repair (OR 2.86, 95% CI 1.72–4.73, $p < 0.0001$) and replacement (OR 2.33, 95% CI 1.55–3.55, $p < 0.0001$), no use of topical ice slush (OR 1.29, 95% CI 1.10–1.49, $p < 0.0009$), and use of inotropic agents for greater than 30 minutes after termination of cardiopulmonary bypass (OR 1.36, 95% CI 1.16–1.59, $p < 0.0001$). Postoperative median ICU stay (3.6 days AF vs. 2 days no AF, $p < 0.001$) and hospital stay (10 days AF vs. 7 days no AF, $p < 0.001$) were higher in AF. Morbid events, hospital mortality, and 6-month mortality were significantly higher in AF ($p < 0.001$): ICU readmission 13% AF vs. 3.9% no AF, perioperative myocardial infarction 7.41% AF vs. 3.36% no AF, persistent congestive heart failure 4.57% AF vs. 1.4% no AF, reintubation 10.59% AF vs. 2.47% no AF, stroke 5.26% AF vs. 2.44% no AF, hospital mortality 5.95% AF vs. 2.95% no AF, 6-month mortality 9.36% AF vs. 4.17% no AF.

Conclusions

Atrial fibrillation after cardiac surgery occurs in approximately one third of patients and is associated with an increase in adverse events in all measurable outcomes of care and increases the use of hospital resources and, therefore, the cost of care. Strategies to reduce the incidence of AF after cardiac surgery should favorably affect surgical outcomes and reduce utilization of resources and thus lower cost of care.

After open cardiac procedures, postoperative arrhythmias are rather common.^{1–4} The majority of these rhythm disturbances are supraventricular, mainly atrial fibrillation (AF) and atrial flutter.^{3–5} Postoperative AF has been regarded, by some, to be a benign, transient, and self-limited arrhythmia⁶ and of no consequence.^{7,8}

Postoperative AF adversely affects the surgical morbidity and mortality and consequently leads to a longer hospital stay and more use of resources, driving up the cost of care.^{1,2,9,10} Both prospective and retrospective studies have tried to identify factors associated with and/or contributing to the genesis of postoperative AF.^{1,2,10–12} A variety of interventions have been sought to treat and prevent the emergence of this arrhythmia with various degrees of success.^{4,13–20}

The current study was conducted to determine the incidence of postoperative AF in a large group of patients undergoing a variety of open cardiac surgery in the Department of Veterans Affairs, identify preoperative, perioperative, and postoperative factors that have significant association with the development of postoperative AF, and to evaluate its impact on patients' outcome.

MATERIALS AND METHODS

Processes, Structures and Outcomes of Care in Cardiac Surgery (PSOCS) is a multicenter Department of Veterans

Affairs cooperative study evaluating the impact of processes and structures of care on the outcome of surgery in patients undergoing open cardiac procedures at 14 participating Veterans Affairs Medical Centers (Appendix I). Data for this observational study are prospectively collected by a dedicated research nurse at each participating institution. Approximately 1500 variables are collected for each patient. For this report, 86 variables, which included preoperative patient demographics, intraoperative practice parameters, and postoperative outcome measures, were analyzed (Appendix II). These variables were selected based on the existing literature and clinical practice data pointing to a possible association with postoperative AF.

Patients

A total of 4184 patients entered the study between September 20, 1993, and December 31, 1996. This represents approximately 57% of the total patients undergoing cardiac surgery at participating institutions during the same period. The study patients were selected using a systematic sample. Each week, a different day was chosen as a starting point. The first three to four patients undergoing cardiac surgery starting on that day then were selected. Urgent–emergent surgeries were oversampled to ensure that enough of this type of patient was entered into the database. A total of 329 patients were excluded from data analysis. Of these, 176 patients had preoperative AF. In 105 patients, the preoperative primary rhythm was unknown, and in the remaining 48 patients, the data for postoperative AF were missing. A total of 3855 patients formed the study population. Each patient was interviewed and examined by the research nurse before surgery. Patients also were seen at 6 months follow-up by

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Table 1. SIGNIFICANT VARIABLES ON UNIVARIATE ANALYSIS ASSOCIATED WITH ATRIAL FIBRILLATION ($p < 0.2$)

Continuous Variables	No Atrial Fibrillation	Atrial Fibrillation	p Value
Age (yr)	62.4 ± 9.7	66.8 ± 8.3	0.0001
Systolic blood pressure (mmHg)	129.5 ± 20.0	131.9 ± 19.8	0.0005
Diastolic blood pressure (mmHg)	72.5 ± 12.1	71.4 ± 11.9	0.0078
Pulse (beats/min)	71.1 ± 13.2	70.1 ± 13.1	0.0300
Creatinine (mg/dL)	1.3 ± 0.8	1.3 ± 0.8	0.0485
Hemoglobin (g/dL)	13.9 ± 1.8	13.6 ± 1.8	0.0001
Ischemic time (hr)	1.2 ± 0.6	1.3 ± 0.7	0.0016
Total cardiopulmonary bypass time (hr)	2.0 ± 0.8	2.1 ± 0.9	0.0001
Smoking (pack-years)	40.3 ± 35.2	42.5 ± 38.4	0.1024

the research nurse, at which time a detailed examination and appropriate laboratory tests were performed.

Statistical Methods

A total of 79 clinical and laboratory risk factors and perioperative measurements were evaluated for their possible associations with the onset of postoperative AF. The one-way analysis of variance was used to compare AF rates for the type of cardiac surgery performed. The *t* test was used to compare values of continuous variables between patients in whom AF developed *versus* those in whom AF did not develop. Comparisons of dichotomous or categorical variables used the chi square test. The log-rank test was used to compare intensive care unit (ICU) and postoperative lengths of stay. Patients who died in the ICU or before discharge from the hospital were excluded from these comparisons. All tests were two sided. Variables with $p < 0.20$ from these univariate analyses (Tables 1 and 2) were selected for possible inclusion in a logistic regression analysis. These variables were entered into a stepwise logistic regression model. The *p* values of 0.05 were used to both enter and eliminate variables. The odds ratio (OR) and 95% confidence interval (CI) for each independent variable in the final regression model are presented.

RESULTS

Patient characteristics are listed in Table 3. The majority were men (98.4%) with an average age of 63.7 ± 9.6 years (range, 25–88 years). Patients younger than 60 years constituted only approximately 28% of the total population. Age distribution is represented by Figure 1. Table 4 lists the surgical procedures performed. Coronary

artery bypass grafting (CABG) as the sole operative procedure was performed in 3126 (81%) of patients. Isolated valve surgery (mitral valve replacement [MVR], 41; aortic valve replacement [AVR], 231) were done in 272 (7%) patients. Grouped under other procedures in Table 4 are a variety of surgeries such as aneurysm repair, aortic surgery, and heart transplantation, and they constitute 2.6% of the total patient population.

The overall incidence of AF was 29.6%. The incidence between participating institutions ranged from 13% to 44%. The small sample size at each hospital, however, precluded any meaningful statistical analysis between the hospitals. When considering single cardiac surgery, the incidence of AF was highest for MVR (48.8%) followed by other cardiac surgery (42.4%), aortic valve replacement (32.9%), and CABG (27.6%) (Table 4). In combined procedures, the highest incidence of AF was seen with CABG + MVR (60%), and CABG + other (39%), and CABG + AVR (36.4%) ranked second and third, respectively (Fig. 2, Table 4).

Univariate analysis identified seven patient-related risk factors and two processes-of-care variables from the category of continuous variables as having high association with postoperative AF (Table 1). Age was the most significant factor. The older patients had a higher likelihood of having AF develop ($p < 0.0001$). An elevated resting systolic blood pressure, a lower diastolic blood pressure, and a slower pulse rate were all significant patient risk factors. A longer cardiopulmonary bypass time and aortic cross-clamping time (ischemic time) also were significant contributors ($p < 0.0001$ and $p < 0.0016$, respectively).

In the group of categorical variables, a large number of variables showed significant association with postoperative AF (Table 2). A history of cerebrovascular and peripheral vascular disease and chronic obstructive pulmonary disease were important markers for development of postoperative AF, as was New York Heart functional class. Preoperative use of digoxin, bronchodilators, and diuretics also was an important predictor on univariate analysis. Preoperative use of β -blockers was not associated with a lesser incidence of AF.

Stepwise logistic regression analysis identified ten independent factors as predictors of postoperative AF (Table 5). From preoperative variables, increasing age was the strongest predictor of AF with an OR of 1.6 for each decade of additional age beyond 50 (95% CI 1.48–1.75, $p < 0.0001$) (Fig. 3). Baseline resting hypertension with a systolic blood pressure above 120 mmHg and a low resting pulse rate below 80 were significant markers of AF ($p < 0.02$ and 0.009, respectively). Chronic obstructive pulmonary disease (COPD) as defined by a preoperative forced expiratory volume in 1 second (FEV₁) < 1.5 L and the use of digoxin

Table 2. SIGNIFICANT VARIABLES ON UNIVARIATE ANALYSIS ASSOCIATED WITH ATRIAL FIBRILLATION ($p < 0.2$)

Categorical Variables	No Atrial Fibrillation (%)	Atrial Fibrillation (%)	p Value
History of cerebrovascular disease	16.82	20.65	0.005
History of peripheral vascular disease	25.05	29.05	0.010
History of COPD	13.51	19.51	0.001
Angina Functional Class	63.91	57.59	0.001
New York Heart Association Function Class	38.81	43.18	0.013
Calcium channel blocking agent use	46.73	51.68	0.005
Diuretic use within 2 wk	25.39	33.81	0.001
Digoxin use within 2 wk	10.82	17.50	0.001
Bronchodilator therapy within 2 wk	12.49	16.80	0.001
Cardiomegaly	19.76	22.66	0.047
Left ventricular hypertrophy	13.44	17.26	0.003
Left bundle branch block	03.56	04.98	0.046
Warm antegrade cardioplegia	28.04	32.08	0.012
Topical ice slush	47.70	41.81	0.001
Composition of cardioplegia	76.30	80.05	0.011
Cardiac venting techniques			
Aorta	65.68	56.54	0.001
Right superior pulmonary vein	25.05	35.03	0.001
Aortic valve replacement	11.85	14.87	0.010
Mitral valve replacement	01.92	04.65	0.001
Mitral valve repair	01.26	03.37	0.001
Tricuspid valve repair	00.15	00.62	0.013
No inotropic agents/devices used for ≥ 30 min	44.00	33.83	0.001
Dopamine	23.63	27.77	0.007
Dobutamine	21.03	27.68	0.001
Epinephrine	14.08	16.78	0.032
Norepinephrine	05.61	08.70	0.001
Amrinone	04.53	06.95	0.002
Other inotrope used	04.23	05.72	0.046
No inotropic agents/devices used for > 1 hr during first 24 hr	38.93	26.82	0.001
Sex (male)	98.27	98.86	0.172
Long-acting nitrates used	60.42	63.22	0.104
Pulmonary or alveolar infiltrate	03.12	04.30	0.076
Cold antegrade cardioplegia	89.81	88.34	0.176
Method of cardioplegia	89.34	91.56	0.093
No cardiac venting techniques used	04.30	05.44	0.126

COPD = chronic obstructive pulmonary disease.

within 2 weeks preceding the operation also were independent predictors of AF (OR 1.37, $p < 0.001$ for COPD and OR 1.37, $p < 0.003$ for digoxin use). Intraoperative variables associated with AF included venting the left ventricle via the right superior pulmonary vein (RSPV) (OR 1.42, $p < 0.0001$) and surgery on the mitral valve. Mitral valve repair (OR 2.86, $p < 0.0001$) and MVR (OR 2.33, $p < 0.0001$) had the strongest association with postoperative AF. The third intraoperative predictor of AF included lack of use of topical ice slush (OR 1.29, $p < 0.0009$). The need for inotropic agents for greater than 30 minutes after termination of cardiopulmonary bypass (OR 1.3.6, $p < 0.0001$) was the other predictor of AF.

Postoperative AF was associated with a higher incidence of morbid events (Table 6). The rate of stroke

(5.26% AF vs. 2.44% no AF) and perioperative myocardial infarction (MI) (7.41% AF vs. 3.36% no AF) was twice as high as in those in whom AF did not develop. The rate of readmission to the ICU (13.49% AF vs. 3.52% no AF), persistent congestive heart failure symptoms (4.57% AF vs. 1.40% no AF), and need for reintubation and ventilatory support (10.59% AF vs. 2.47% no AF) tripled in patients with postoperative AF (Table 4).

The median stay in the ICU and the postoperative hospital stay were 3.6 and 10 days, respectively, in patients with postoperative AF versus 2 days and 7 days, respectively, for patients with no postoperative AF ($p < 0.001$).

Both in-hospital mortality (5.95%) and mortality at 6 months (9.36%) after surgery were significantly

Table 3. PATIENT DEMOGRAPHICS

	No Atrial Fibrillation (n = 2712)		Atrial Fibrillation (n = 1143)		p Value
	n	%	n	%	
Age (yr, mean \pm SD)	62.4 \pm 9.7		66.8 \pm 8.3		0.0001
Sex					0.172
Male	2664/3794	70.2	1130/3794	29.8	
Female	47/60	78.3	13/60	21.7	
IDDM	315/2715	11.6	131/1149	11.4	0.858
COPD	366/2710	13.5	223/1143	19.5	0.001
Prior MI	1377/2565	53.7	595/1062	56.0	0.198
Prior heart surgery	285/2711	10.5	122/1143	10.7	0.882
Hypertension	1571/2711	58.0	702/1143	61.4	0.046
Current smoker	771/2697	28.6	241/1138	21.2	0.001
β -blocker use	1598/2696	59.3	667/1130	59.0	0.887
Digoxin use within 2 wk	289/2672	10.8	196/1120	17.5	0.001

IDDM = insulin dependent diabetes mellitus; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction.

higher in patients with postoperative AF compared to 2.95% and 4.18%, respectively, for patients with no AF ($p < 0.002$ for hospital mortality and $p < 0.001$ for 6 months' mortality).

DISCUSSION

The incidence of AF in general populations is approximately 1.8%.²¹ It is only 0.4% for individuals younger than 70 years of age and rises to 2% to 4% for those older than 70 years of age.²² In patients undergoing general surgical procedures, the incidence is approximately 5%.^{23,24} In hospitalized patients, this prevalence is between 8% and 14%.²⁵ For patients undergoing open cardiac procedures, the reported incidence of AF is clearly much higher, ranging from 3.1% to 91%, with most large series reporting an incidence around 30%.^{1,2,4,6,10-13,15,17,26-28} Certain patients appear to have a higher risk of having AF develop.³ The current study shows an average incidence of 29.6% for postoperative AF. Among the 14 participating centers in

this study, the incidence of AF varied between 13% and 44% with the majority of hospitals having an incidence from 20% to 30%. The difference in AF incidence could not be explained based on the number and type of operative procedures, as valvular surgery, for example, constituted approximately 7% to 10% of surgery for most centers.

In the past, this arrhythmia was thought to be a self-limiting, transient, and benign rhythm disturbance.^{6,7} Yet, as more information has accumulated through multiple studies, it has become evident that postoperative AF is a major contributing factor or marker of increasing postoperative morbidity and mortality.^{1,2,10,29,30}

The etiology of postoperative AF remains unclear, although a multiplicity of factors such as surgical trauma,³¹ lack of adequate preservation of atrial tissue by cardi-

Table 4. INCIDENCE OF ATRIAL FIBRILLATION BY TYPE OF OPERATIVE PROCEDURE

Operation	Number of Patients	Atrial Fibrillation (%)
Single operations		
CABG	3126	27.6
AVR	231	32.9
Other	99	42.4
MVR	41	48.8
Combined operations		
CABG + AVR	228	36.4
CABG + other	95	39
CABG + MVR	35	60

CABG = coronary artery bypass grafting; AVR = aortic valve replacement; MVR = mitral valve replacement.

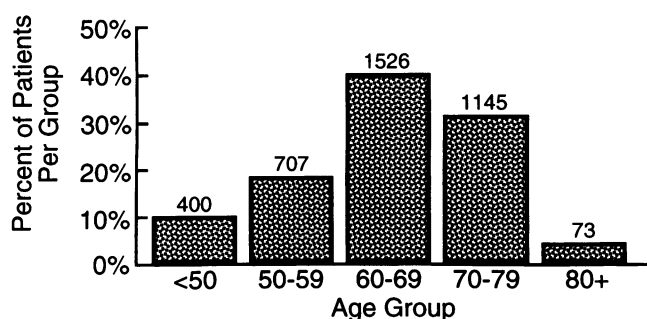


Figure 1. Age distribution of patients. The majority (72%) are older than 60 years.

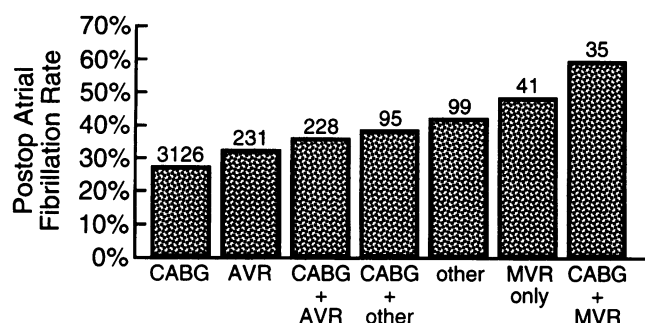


Figure 2. Postoperative atrial fibrillation rate according to the surgical procedure. Coronary artery bypass grafting (CABG) + mitral valve replacement has the highest incidence rate (60%). CABG = coronary artery bypass surgery; MVR = mitral valve replacement; AVR = aortic valve replacement.

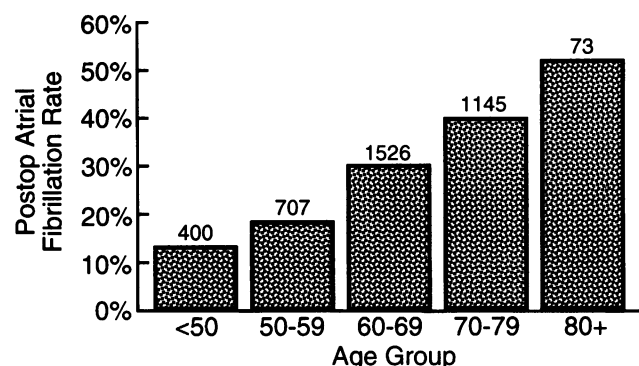


Figure 3. Relation between increasing age and postoperative atrial fibrillation. Older patients have a higher rate of postoperative atrial fibrillation.

oplegia,³² inadequate cooling of atrium,^{33,34} postoperative pericarditis,³¹ withdrawal of preoperative β -blockers,²⁰ increased sympathetic activity,¹² euthyroid sick syndrome,¹³ and many more have been proposed as responsible for the genesis of AF. The hypothesis of "dispersion of refractoriness" appears more plausible, in which dispersion or lack of uniformity of local atrial refractory periods is thought to be the mechanism underlying the vulnerability of atrial tissue toward the development of AF.³

Depending on the patient's age, the incidence of AF varied from 13% for patients younger than 50 years of age to 52% for those 80 years of age or older (Fig. 2), with an OR of 1.60 for each decade of additional life (Table 3). This is in agreement with other reports in which older age consistently has been found to be a predictor of postoperative AF.^{1,2,10,11,25,27,31,32} Older age may cause structural changes in the heart such as an increase in chamber size and fibrosis.³⁵ Senile cardiac amyloidosis was seen in 66% of an autopsy series.³⁵ It was limited to the atria in approximately two thirds of these patients.³⁵ In addition, the majority of these patients suffer from high

blood pressure with secondary cardiac hypertrophy that, combined with senescent changes in myocardium, can provide a suitable substrate for generation of AF.²

From preoperative patients' variables, a high systolic blood pressure was associated with postoperative AF. Hypertension was present in 60% of patients with AF in the Framingham Study.²¹ Only one prior prospective study² has shown the association between preoperative hypertension and postoperative AF. Hypertension leads to myocardial hypertrophy. These hearts may contain foci of myocardial fibrosis,³⁵⁻³⁷ as well as abnormal electrophysiologic properties³⁸ acting as substrates and contributing factors toward the emergence of AF.

Hospitalized patients with COPD have as high an incidence of arrhythmias as 89%.³⁹ These patients have a ventilation perfusion (V/Q) mismatch that can lead to arterial hypoxia. Poor ventilatory mechanics and atelectasis of the lung in the postoperative period will aggravate this V/Q mismatch and hypoxia. Atrial fibrillation decreases the cardiac output and leads to further deterioration of hypoxemia that can be fatal if not corrected. These

Table 5. SIGNIFICANT VARIABLES ASSOCIATED WITH ATRIAL FIBRILLATION

Variable	Odds Ratio*	95% Confidence Interval	p Value
MV repair	2.86	1.72, 4.73	0.0001
MV replacement	2.33	1.53, 3.55	0.0001
Age group	1.61	1.48, 1.75	0.0001
Venting via right superior pulmonary vein	1.42	1.21, 1.67	0.0001
History of COPD	1.37	1.12, 1.66	0.0016
Use of digoxin within 2 wk of surgery	1.37	1.10, 1.70	0.0039
Inotropes >30 min, post CPB	1.36	1.16, 1.59	0.0001
No topical ice slush	1.29	1.10, 1.49	0.0009
Pulse <80	1.26	1.06, 1.51	0.0094
SBP >120	1.19	1.02, 1.40	0.0266

MV = mitral valve; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; SBP = systolic blood pressure.

* OR was 1.6 for each decade of life beyond 50 years.

Table 6. RELATIONSHIP OF POSTOPERATIVE EVENTS TO ATRIAL FIBRILLATION

Event	No Atrial Fibrillation (n = 2712)		Atrial Fibrillation (n = 1143)		P Value*
	n	%	n	%	
Readmission to ICU	95/2696	3.5	153/1134	13.5	0.001
Perioperative MI	91/2708	3.4	84/1133	7.4	0.001
Persistent CHF symptoms	38/2709	1.4	52/1138	4.6	0.001
Stroke	66/2709	2.4	60/1141	5.3	0.001
Reintubation	67/2709	2.5	121/1143	10.6	0.001
30-day mortality	80/2712	3.0	68/1143	6.0	0.001
6-mo mortality	113/2712	4.2	107/1143	9.4	0.001
Median stay (days)					
ICU	2692	2.0	1138	3.6	0.001
Postoperative	2679	7.0	1134	10.0	0.001

CHF = congestive heart failure; MI = myocardial infarction.

* Chi square analysis.

patients have frequent premature atrial contractions that predispose them to AF.¹ The COPD proved to be a predictor of AF (OR 1.36, CI 1.12–1.65). A similar association between COPD and AF was found by Leitch et al.²⁷ in their retrospective review of 5807 patients who underwent CABG in an earlier era.

In the past, preoperative use of digoxin was thought to be effective in reducing the rate of AF.¹⁵ Multiple studies, however, have shown the ineffectiveness of digoxin in this regard.^{4,14,40} In the study by Roffman and Fieldman,⁴¹ only the combination of digoxin and β -blockers was found effective in reducing the incidence of AF. Our study, however, indicates that the use of digoxin within 2 weeks before cardiac operation is a significant contributing factor to the development of AF. This is in contrast to the findings of Hashimoto et al.⁴² This probably is because of the presence of pre-existing cardiac conditions such as congestive heart failure or arrhythmia, necessitating digoxin use, but could be the result of digoxin itself sensitizing the myocardium.⁴³ The group from Barnes Hospital found similar association between preoperative digoxin usage and AF.¹

The use of β -blockers starting in the preoperative period has been shown to decrease the incidence of postoperative AF.^{4,7,10,27} The preoperative use of β -blocking agents in our patients had no relation to the development of AF. This may be because our study was not specifically designed to look at this issue.

Intraoperative variables associated with AF included venting the left ventricle via the RSPV and mitral valve repair or replacement. Mathew et al.¹⁰ found LV venting through the RSPV also to be a contributing factor (onefold–fourfold

increase in the OR) to the increased rate of AF. Whether this is related to local trauma at the insertion site to the thicker atrial muscle bundles between and around the orifices of pulmonary veins¹⁰ or is being used in patients who are showing left ventricular dysfunction and, therefore, an outcome rather than a predictive variable remains speculative. Analysis of our data showed that RSPV venting was used in 66% of patients undergoing aortic valve surgery and in 33% of patients requiring mitral valve operations, yet the incidence of AF was higher for mitral valve procedures. It therefore appears that the cause of AF with RSPV venting is related to other factors. The current data suggest aortic root venting to be superior than venting via the RSPV, as the former appeared to be protective against AF on univariate analysis ($p < 0.001$) (Table 2), although it did not attain statistical significance ($p > 0.05$) in the logistic regression model.

Mitral valve repair and replacement, usually, mandates bicaval cannulation and dissection in the interatrial groove. Bicaval cannulation has been shown to increase the incidence of postoperative AF.¹⁰ By the nature of the surgery, these procedures also may require longer times of cardiopulmonary bypass and aortic cross-clamping. These may confound the effect of mitral valve surgery itself on the emergence of postoperative AF. From our data, we could not separate the effects of bicaval cannulation from those of valve surgery. Cardiopulmonary bypass time and ischemic time were not significant contributors to AF on logistic regression analysis.

The lack of use of topical ice slush was found to be a significant predictor for AF (OR 1.24, CI 1.11–1.50, $p < 0.0010$). Thirty-two percent of patients in whom ice slush was not used had AF develop *versus* 27% when ice slush was used ($p < 0.001$). Our study is the first to show the positive effect for the use of ice slush and myocardial cooling on the incidence of AF in a large clinical series. Warming of the atrial tissue during cardioplegic arrest with continued electrical activity in the atria has been blamed for high incidence of AF.³³ Smith et al.,³⁴ in their experimental studies, found that although the ventricular septum rapidly cooled down to 8 C after the initial infusion of cardioplegic solution, the atrial septum cooled to only 22 C with rapid rewarming within 3 to 5 minutes after completion of initial cardioplegia infusion. Inadequate cooling of atrial tissue allows anaerobic metabolism to continue in a cardioplegic, arrested heart. Although continued electrical activity in the atrium does not require large amounts of energy (only 1% of that used by the working heart)⁴⁴ and, therefore, should not lead to anaerobic metabolism, it is conceivable that this may be a marker of undetected mechanical activity that can rapidly deplete the energy stores.³³ Our data imply that cooling of the atrial tissue with topical ice slush along with multidose cardioplegia during the aortic cross-clamping may protect the atrial tissue and decrease the incidence of postopera-

tive AF. If this technique is used, however, care must be taken to protect the phrenic nerve.

The need for using inotropic agents in the postoperative period is related to two major factors: 1) the preoperative degree of myocardial dysfunction and 2) intraoperative events such as inadequate myocardial protection, incomplete revascularization, and technical difficulties. Some surgeons routinely use inotropic agents when weaning the patient from cardiopulmonary bypass. This makes it rather difficult to know if the use of inotropic agents was because of the surgeon's habit or a result of myocardial dysfunction. Our data show that if inotropic support was needed beyond 30 minutes after termination of cardiopulmonary bypass, then the rate of AF was significantly higher. The data also showed that the use of inotropic agents for more than 1 hour, in the first 24 hours after surgery, was associated with a higher incidence of AF. This, however, can be an outcome event rather than a marker for AF.

The postoperative morbid events were all increased with AF. The readmission rate to the ICU, persistent symptoms of congestive heart failure, and need for reintubation were almost tripled in patients with AF. The relation of whether the presence of congestive heart failure or respiratory insufficiency contributed to the development of AF or was caused by it is difficult to determine. For example, could fluid overload in the perioperative period contribute to the development of AF or does fluid retention occur as a consequence of AF? As a whole, patients with AF had a longer median stay in the ICU (3.6 days vs. 2 days with no AF). This may be related to the need for stabilization of hemodynamic status, correction of hypoxia, need for ventilatory support, or a combination of all. Other authors^{1,2,10} have found similar association.

The most devastating complication of AF, aside from mortality, is the increased rate of stroke, which was 5.3% in the current study, almost double the rate of stroke in patients without AF. This is in agreement with other studies in the literature.^{1,2,6,29,30} The AF increases the risk of stroke by fivefold.⁴⁵ This risk is independent of the associated cardiac failure and coronary artery disease. In patients with nonvalvular heart disease, Sage and Van Uitert⁴⁶ found that the recurrence rate for stroke with AF after the initial stroke was 20% per year with no difference between chronic and intermittent AF. The mortality from stroke was 38%. Taylor et al.²⁹ in a consecutive series of 500 patients found a 7% incidence of stroke in patients with AF *versus* 1% without AF. Creswell et al.¹ found a 3.3% stroke rate with postoperative atrial arrhythmias compared to 1.4% in those without such rhythm disturbances. The mortality in this series, however, was not higher for patients with stroke. The physical disability and its devastating consequences for the patient and family as well as the drain that it puts on the use of resources with

consequent increase in the cost of hospitalization make it imperative to design strategies to prevent the emergence of AF, to treat it effectively once it develops, and to initiate prophylactic anticoagulation protocols for prevention of embolic strokes.⁴⁶

The rate of perioperative MI was more than double in patients with AF (7.41% AF vs. 3.36%, $p < 0.001$) (Table 6). This, however, could be misleading as in almost all patients in whom AF develop, an electrocardiogram and cardiac enzymes invariably will be obtained, which can increase the detection rate of MI compared to patients in sinus rhythm in whom these tests are not routinely performed after surgery. Perioperative MI with a left ventricular ejection fraction under 0.4 was found to increase the posthospital discharge mortality (68% event-free survival vs. 92% for those without a perioperative MI).⁴⁷ The current data show an increased rate of perioperative MI as well as a higher mortality rate at 6 months (9.36% AF vs. 4.17%, $p < 0.001$). Part of this increased mortality rate could very well be a result of perioperative MI. This, however, could not be ascertained from our data.

The need for a longer stay in the ICU and on the nursing ward seen in this series (Table 6) has been observed by other investigators as well.^{1,2,10} The AF increased the median postoperative hospital stay from 7 days to 10 days. Although we did not analyze the actual hospital costs per patient, it is clear that a 4-day increase in hospital stay will have significantly driven up the cost of hospitalization. The additional cost was estimated to be approximately \$10,055 to \$11,500 per patient in a non-Veterans Administration hospital.²

Limitations

There are several limitations to our study. First, the study was not designed specifically to look at postoperative AF. As such, we could not establish with certainty a direct causality between the predictors listed and postoperative AF. Second, we could not determine the exact timing of postoperative events such as AF and neurologic events or MI from our data. It is therefore difficult to establish a temporal relation between these events and AF. Third, the majority of our patients (98.4%) were male; therefore, the effect, or lack thereof, of sex on AF could not be evaluated. Fourth, the higher rate of MI with AF may be related to the fact that cardiac enzymes and electrocardiograms were obtained in these patients, but not in those with sinus rhythm. Our study, however, has the advantage of a 6-month follow-up showing an increased mortality rate for patients with postoperative AF.

In conclusion, AF remains the most common complication after open cardiac procedures. A number of preoperative patient characteristics and intraoperative practice variables appear to affect the incidence of this

arrhythmia. Older age continues to be a significant predictor, as are the presence of COPD, hypertension, and use of digoxin before surgery. The measurable outcomes of care (*i.e.*, perioperative MI, stroke, persistent congestive heart failure, need for reintubation, ventilatory support, and longer ICU stay) are all associated with postoperative AF, leading to increased resource utilization. Long-term survival is adversely affected by AF. Strategies to identify the patients at risk and to modify these risk factors by aggressive prophylactic measures as well as changes in surgical techniques should lead to a lower incidence of AF and a reduced morbidity and mortality rate for patients undergoing cardiac surgery.

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References

- Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of post-operative atrial arrhythmias. *Ann Thorac Surg* 1993; 56:539–549.
- Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery: current trends and impact on hospital resources. *Circulation* 1996; 94:390–397.
- Cox JL. A perspective of post-operative atrial fibrillation in cardiac operations. *Ann Thorac Surg* 1993; 56:405–409.
- Rubin DA, Nieminski KE, Reed GE, Herman MV. Predictors, prevention, and long-term prognosis of atrial fibrillation after coronary artery bypass graft operations. *J Thorac Cardiovasc Surg* 1987; 94:331–335.
- Moore SL, Wilkoff BL. Rhythm disturbances after cardiac surgery. *Semin Thorac Cardiovasc Surg* 1991; 3:24–28.
- Chung MK, Asher CR, Dykstra D, et al. Does post-operative atrial fibrillation predispose to stroke, embolic events, or death after coronary artery bypass grafting? *Circulation* 1995; 92:I–644.
- Fuller JA, Adams GG, Buxton B. Atrial fibrillation after coronary artery bypass grafting: is it a disorder of the elderly? *J Thorac Cardiovasc Surg* 1989; 97:821–825.
- Lauer MS, Eagle KA, Buckley MJ, DeSanctis RW. Atrial fibrillation following coronary artery bypass surgery. *Prog Cardiovasc Dis* 1989; 31:367–378.
- Mathew JP, Parks R, Friedman A, et al. Post-operative atrial fibrillation in patients undergoing coronary artery bypass grafting (CABG) surgery: predictors, outcomes, and cost. *Anesth Analg* 1995; 80:SCA48.
- Mathew JP, Parks R, Savino JS, et al. Atrial fibrillation following coronary artery bypass graft surgery. *JAMA* 1996; 276:300–306.
- Mendes LA, Connelly GP, McKenney PA, et al. Right coronary artery stenosis: an independent predictor of atrial fibrillation after coronary artery bypass surgery. *J Am Coll Cardiol* 1995; 25:198–202.
- Kalman JM, Munawar M, Howes LG, et al. Atrial fibrillation after coronary artery bypass grafting is associated with sympathetic activation. *Ann Thorac Surg* 1995; 60:1709–1715.
- Klemperer JD, Klein IL, Ojamaa K, et al. Triiodothyronine therapy lowers the incidence of atrial fibrillation after cardiac operations. *Ann Thorac Surg* 1996; 61:1323–1329.
- Fanning WJ, Thomas Jr CS, Roach A, et al. Prophylaxis of atrial fibrillation with magnesium sulfate after coronary artery bypass grafting. *Ann Thorac Surg* 1991; 52:529–533.
- Parker FB, Greiner-Hayes C, Bove EL, et al. Supraventricular arrhythmias following coronary artery bypass: the effect of pre-operative digitalis. *J Thorac Cardiovasc Surg* 1983; 86:594–600.
- McAlister HF, Luke RA, Whitlock RM, Smith WM. Intravenous amiodarone bolus versus oral quinidine for atrial flutter and fibrillation after cardiac operations. *J Thorac Cardiovasc Surg* 1990; 99:911–918.
- Suttrop MJ, Kingma JH, Gin MTJ, et al. Efficacy and safety of low- and high-dose sotalol versus propranolol in the prevention of supraventricular tachyarrhythmias early after coronary artery bypass operations. *J Thorac Cardiovasc Surg* 1990; 100:921–926.
- Stephenson LW, MacVaugh III H, Tomasello DN, Josephson ME. Propranolol for prevention of post-operative cardiac arrhythmias: a randomized study. *Ann Thorac Surg* 1980; 29:113–116.
- Yilmaz AT, Demirkilic U, Arslan M, et al. Long-term prevention of atrial fibrillation after coronary artery bypass surgery: comparison of quinidine, verapamil, and amiodarone in maintaining sinus rhythm. *J Card Surg* 1996; 11:61–64.
- White HD, Antman EM, Glynn MA, et al. Efficacy and safety of timolol for prevention of supraventricular tachyarrhythmias after coronary artery bypass surgery. *Circulation* 1984; 70:479–484.
- Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: The Framingham Study. *N Engl J Med* 1982; 306:1018–1022.
- Alpert JS, Petersen P, Godtfredsen J. Atrial fibrillation: natural history, complications, and management. *Annu Rev Med* 1988; 39:41–52.
- Goldman L. Supraventricular tachyarrhythmia in hospitalized adults after surgery. Clinical correlates in patients over 40 years of age after major non cardiac surgery. *Chest* 1978; 73:450–454.
- Johnston KW. Multicenter prospective study of nonruptured abdominal aortic aneurysm. Part II. Variables predicting morbidity and mortality. *J Vasc Surg* 1989; 9:437–447.
- Flaker GC. Atrial fibrillation: new ideas on an old arrhythmia. *Cardiovasc Rev Rep* 1990; 12:23–29.
- Smith R, Grossman W, Johnson L, et al. Arrhythmias following cardiac valve replacement. *Circulation* 1972; 45:1018–1023.
- Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1990; 100:338–342.
- Gavaghan TP, Campbell TJ, Feneley MP, Morgan JJ. Atrial tachyarrhythmias after cardiac surgery: results of disopyramide therapy. *Aust N Z J Med* 1985; 15:27–32.
- Taylor GJ, Malik SA, Colliver JA, et al. Usefulness of atrial fibrillation as a predictor of stroke after isolated coronary artery bypass grafting. *Am J Cardiol* 1987; 60:905–907.
- Reed GL, Singer DE, Picard EH, DeSanctis RW. Stroke following coronary-artery bypass surgery. A case-control estimate of the risk from carotid bruits. *N Engl J Med* 1988; 319:1246–1250.
- Angelini P, Feldman MI, Lufschanowski R, Leachman RD. Cardiac arrhythmias during and after heart surgery: diagnosis and management. *Prog Cardiovasc Dis* 1974; 16:469–495.
- Tchervenkov CI, Wynands JE, Symes JF, et al. Persistent atrial activity during cardioplegic arrest: a possible factor in the etiology of post-operative supraventricular tachyarrhythmias. *Ann Thorac Surg* 1983; 36:437–443.
- Chen X, Newman M, Rosenfeldt FL. Internal cardiac cooling improves atrial preservation: electrophysiological and biochemical assessment. *Ann Thorac Surg* 1988; 46:406–411.
- Smith PK, Buhman WC, Levett JM, et al. Supraventricular conduction abnormalities following cardiac operations: a complication of

- inadequate atrial preservation. *J Thorac Cardiovasc Surg* 1983; 85:105–115.
35. Lie JT, Hammond PI. Pathology of the senescent heart: anatomic observations on 237 autopsy studies of patients 90 to 105 years old. *Mayo Clin Proc* 1988; 63:552–564.
 36. Toyoshima H, Park YD, Ishikawa Y, et al. Effect of ventricular hypertrophy on conduction velocity of activation front in the ventricular myocardium. *Am J Cardiol* 1982; 49:1938–1948.
 37. McLenachan JM, Dargie HJ. Ventricular arrhythmias in hypertensive left ventricular hypertrophy. *Am J Hypertens* 1990; 3:735–740.
 38. Topol EJ, Traill TA, Fortuin NJ. Hypertensive hypertrophic cardiomyopathy of the elderly. *N Engl J Med* 1985; 312:277–283.
 39. Holford FD, Mithoefer JC. Cardiac arrhythmias in hospitalized patients with chronic obstructive pulmonary disease. *Am Rev Resp Dis* 1973; 108:879–885.
 40. Weiner B, Rheinlander HF, Decker EL, Cleveland RJ. Digoxin prophylaxis following coronary artery bypass surgery. *Clin Pharm* 1986; 5:55–58.
 41. Roffman JA, Fieldman A. Digoxin and propranolol in the prophylaxis of supraventricular tachydysrhythmias after coronary artery bypass surgery. *Ann Thorac Surg* 1981; 31:496–501.
 42. Hashimoto K, Ilstrup DM, Schaff HV. Influence of clinical and hemodynamic variables on risk of supraventricular tachycardia after coronary artery bypass. *J Thorac Cardiovasc Surg* 1991; 101:56–65.
 43. Rose MR, Glassman E, Spencer FC. Arrhythmias following cardiac surgery: relation to serum digoxin levels. *Am Heart J* 1975; 89:288–294.
 44. Klocke FJ, Braunwald E, Ross J Jr. Oxygen cost of electrical activation of the heart. *Circ Res* 1966; 18:357–365.
 45. Wolf PA, Kannel WB, McGee DL, et al. Duration of atrial fibrillation and imminence of stroke: The Framingham Study. *Stroke* 1983; 14:664–667.
 46. Sage JI, Van Uitert RL. Risk of recurrent stroke in patients with atrial fibrillation and non-valvular heart disease. *Stroke* 1983; 14:537–540.
 47. Force T, Hibberd P, Weeks G, et al. Perioperative myocardial infarction after coronary artery bypass surgery: clinical significance and approach to risk stratification. *Circulation* 1990; 82:903–912.

Appendix I. PARTICIPATING VA MEDICAL CENTERS IN PSOCs STUDY

Institution	Participants
Principal Investigators	
Denver, CO	Karl E. Hammermeister, M.D. (Co-Chairman) Frederick L. Grover, M.D. (Co-Chairman)
Principal Investigator/Research Nurse	
Ann Arbor, MI	Marvin Kirsh, M.D./Connie Newman, R.N.
Asheville, NC	John Lucke, M.D./Sheryl P. Davis, R.N.
Charleston, SC	John Handy, M.D./Lisa A. Colton, R.N.
Denver, CO	David Fullerton, M.D./Janet Baltz, R.N.
Hines, IL	Donald DePinto, M.D./Louise M. Barder, R.N.
Little Rock, AR	Kwabena Mawulawd, M.D./Michael Smith, R.N.
Milwaukee, WI	G. Hossein Almassi, M.D./Tracey Schowalter, R.N.
Minneapolis, MN	Herbert Ward, M.D./Ellie Carson, R.N.
Nashville, TN	Walter Merrill, M.D./Jim Shaw, R.N.
New York, NY	Rick Esposito, M.D./Rosemary A. Mannix, R.N.
San Antonio, TX	O. LaWayne Miller, M.D./Marina Silguero, R.N.
San Diego, CA	Riyad Tarazi, M.D./Cecilia Garcia, R.N.
Tucson, AZ	Gulshan K. Sethi, M.D./Gayle Murad, R.N.
West Roxbury, MA	Shukri Khuri, M.D./Janet E. Bannister, R.N.
Coordinators and Consultants	
Hines, IL (Coordinating Center)	William G. Henderson, Ph.D. (Biostatistician) Thomas E. Moritz, M.S. (National Data Coordinator) Raslan O. Othman, M.S. (Systems Analyst) Lizy G. Thottapurathu, M.S. (Statistical Programmer)
Denver, CO	A. Laurie Shroyer, Ph.D. (Health Services Researcher) Catherine B. VillaNueva, R.N. (National Research Nurse Coordinator) Samantha Ma Whinney, ScD. (Biostatistician)
Northwestern University Chicago, IL	Martin J. London, M.D. (Anesthesia Consultant) Martin J. McCarthy, Ph.D. (Health Research Scientist)

Appendix II. VARIABLES ANALYZED WITH UNIVARIATE ANALYSIS

Age	Permanent pacemaker	Pulmonary artery vented
Sex (male)	Permanent pacemaker	Aortic valve replacement
Systolic blood pressure	Long-acting nitrates used	Mitral valve replacement
Diastolic blood pressure	Pulmonary or alveolar infiltrate	Tricuspid valve replacement
Pulse	Left ventricular hypertrophy	Tricuspid valve repair
History of cerebrovascular disease	Pleural effusion	Aortic valve repair
History of peripheral vascular disease	Pulmonary effusion	LV aneurysmectomy
History of COPD	Pulmonary venous engorgement	Great vessel repair
Angina Functional Class	ECG MI	Coronary bypass grafting
New York Heart Association Function Class	Resting ST segment depression	Lowest myocardial temperature
Diabetes	Severity of aortic stenosis	Lowest systemic temperature
Glucose	Surgical priority	Lowest hematocrit post CPB
Prior heart surgery	Preoperative use of IABP	No inotropic agents/devices used for
Prior MI	Cardiac arrest requiring CPB within 24 hr preceding surgery	≥30 minutes
β-blocker use preoperative	Total CPB time (hr)	Dopamine
Digoxin use within 2 weeks	Ischemic time (hr)	Dobutamine
Diuretic use within 2 weeks	Method of cardioplegia	Epinephrine
Calcium channel blocking agent use	Cold antegrade cardioplegia	Norepinephrine
Bronchodilator therapy within 2 weeks of surgery	No cardiac venting techniques used	Amrinone
Nitroglycerin use within 2 weeks of surgery	Warm antegrade cardioplegia	Other inotrope used
Hemoglobin	Topical ice slush	No inotropic agents/devices used for
Cardiomegaly	Topical cold saline	>1 hr during first 24 hr
Creatine	Heart jacket	ICU stay
Pulmonary rales	Any myocardial temperature monitoring	Hospital stay
Smoking (pack-years)	Myocardial pH monitoring	Readmission to ICU
Alcohol abuse	Composition of cardioplegia	Persistent CHF systems
Current smoker	Cardiac venting techniques: aorta	Perioperative MI
Left bundle branch block	Cardiac venting techniques: left ventricle <i>via</i> right superior pulmonary vein	Stroke
History of liver disease	Left ventricle apex vented	Reintubation
Hepatomegaly	Left atrium right superior pulmonary vein	

COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; IABP = intra-aortic balloon pump; CPB = cardiopulmonary bypass.

Discussion

DR. FRANK C. SPENCER (New York, New York): I appreciate this large amount of work in documenting one of the common hazards after cardiac surgery. And the scary thing is, you can be perfectly well, but arrhythmia can precipitate a stroke from an embolus. So this probably has a potential to be the most disastrous postoperative complication of all.

DR. FREDERICK PARKER (Syracuse, New York): I have enjoyed this paper as it speaks to one of the most troublesome problems in cardiac surgery. In the low-risk patient, it can extend hospital stay, it can lead to early readmission, and often it requires the use of potent antiarrhythmics with significant side effects.

In the high-risk patient the marked decrease in cardiac output after the onset of rapid atrial fibrillation can quickly lead to increased morbidity and even mortality and often requires immediate cardioversion in an extremely ill patient. It also brings up the issue of anticoagulation in the newly postoperative patient, as there is a reported threefold incidence of peripheral emboli and stroke after the onset of fibrillation.

The present series looks at variables that have predictive value for the development of this process. Besides the variables

mentioned, other studies have implicated prolonged aortic cross-clamp times, left ventricular dysfunction, reoperation, and increased bypass time.

Many years ago our own group reported an incidence of atrial fibrillation in the postoperative coronary patient of only 4% using a preoperative regimen of digoxin and propranolol. Nowadays older, higher-risk patients and use of new cardioplegic techniques, as well as a high incidence of reoperations, have brought our own incidence to 20%.

We also feel that the process of right atrial cannulation, use of the right atrium for the delivery of retrograde cardioplegia, and placement of atrial suture lines may also set up foci for reentrant circuits leading to fibrillation.

I have only one question. You implied that the postoperative morbid events are caused by atrial fibrillation. Perioperative infarction and stroke are often intraoperative events. Reintubation can be an early postoperative event. Have your data been screened to assure that these complications definitely occurred postoperatively after the onset of fibrillation?

DR. ALDEN H. HARKEN (Denver, Colorado): I would like to commend Dr. Almassi for his perseverance in putting together a 4000-patient study. The statistical power of this kind of study is huge, obviously. I would also like to commend the authors